Dosimetry and Response Modeling in ^{90}Y-SIRT: Impact of Monte-Carlo SPECT and Segmentation Method

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BACKGROUND

- Treatment planning and dosimetry in ^{90}Y selective internal radiation therapy (^{90}Y-SIRT) rely on accurate determination of perfused volumes (PV)
- Bremsstrahlung ^{90}Y-SPECT imaging remains limited, with poor resolution and erroneous counts throughout the imaging volume
- "Ground truth" definition of treated regions and PVs for dosimetry calculations remains elusive
- Identifying discrepancies between planned and observed treatment regions can provide immediate feedback for cases that may risk poor response – no need to wait for imaging follow-up
- In this work, the impact of different ^{90}Y-SPECT reconstructions and PV segmentation methods on dosimetry and response modeling were assessed

METHODS

- 43 hepatocellular carcinoma (HCC) tumors were treated with ultra-selective radiation segmentectomy using ^{90}Y-SIRT
- The imaging data and dosimetry workflow used are both outlined in **Figure 1** below
- PV segmentation was performed using: 1) HU-threshold guidance from planning-CBCT, and 2) three post-therapy ^{90}Y-SPECT/CT thresholds at 10, 20, and 30 pct of maximum counts
- Two ^{90}Y-SPECT recons were employed: 1) clinical standard and 2) Monte-Carlo (MC) corrected
- Post-therapy, ^{90}Y-SPECT/CT voxelized dosimetry was computed using the local deposition method with activity normalized to the PV
- PV volumes, PV/tumor dose metrics, and dose-response models were compared using the different segmentation and ^{90}Y-SPECT/CT reconstruction strategies

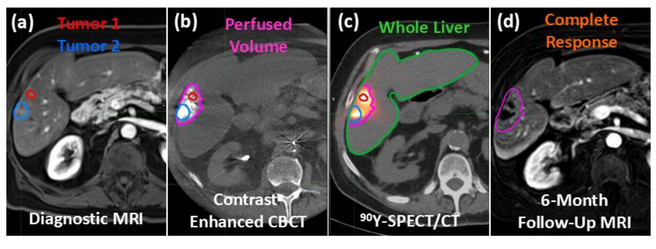


Figure 1. Basic dosimetry/response workflow using CBCT-based PV segmentation: tumor(s) are segmented from the diagnostic MRI (a), then the PV is segmented from the contrast-enhanced CBCT (b), and finally the whole liver from the CT in ^{90}Y-SPECT/CT (c). The tumor and PV contours are rigidly registered and transferred to the ^{90}Y-SPECT/CT in (c) for dosimetry calculations. Voxelized dosimetry estimates were computed from (c) using the local deposition method and activity normalization to the PV from (b). Complete response of both tumors at 6-months follow-up is seen in (d).

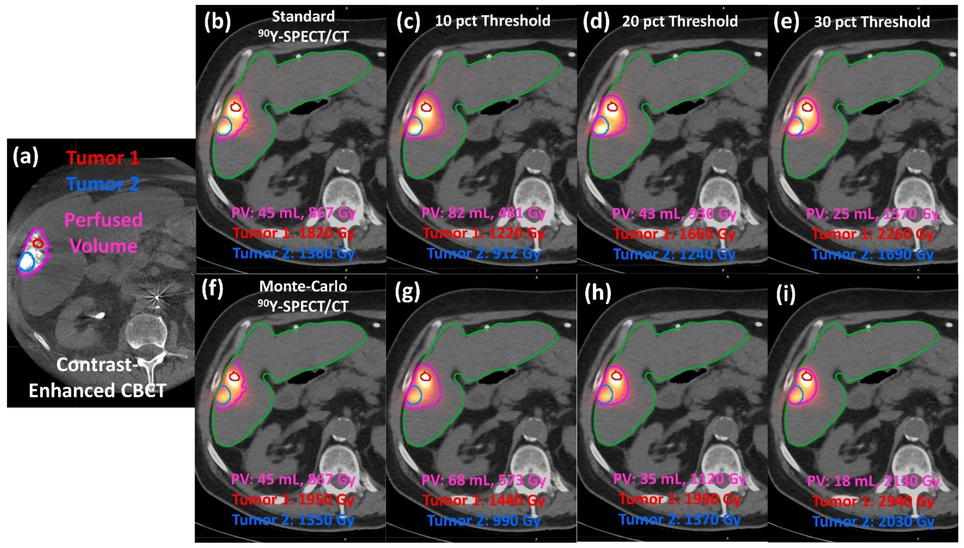
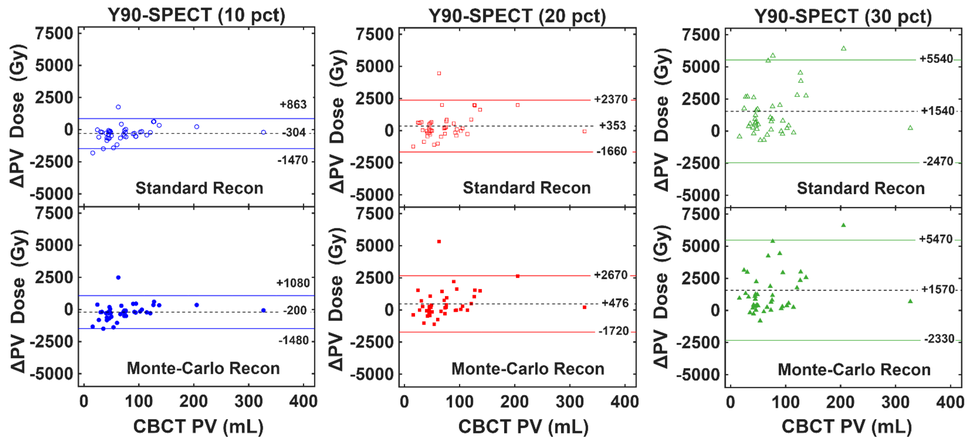


Figure 1. An example case outlining the various methods used to compute PV volumes and dosimetry in this study. The reference PV was determined using from contrast-enhanced CBCT during the planning procedure (a). Tumor and PV contours were transferred and registered to both standard (b-e) and MC-corrected (f-i) ^{90}Y-SPECT/CT. Three different SPECT-based thresholds of 10 (c,g), 20 (d,h), and 30 (e,i) pct of max counts were used to objectively determine the PV for comparison with CBCT segmentation. The PV volumes, PV mean dose, and tumor mean doses derived from each PV segmentation method are included in each figure. In the case highlighted above, PV volumes changed significantly, ranging from 18 mL (i) to 82 mL (c). These differences in PV size then impacted PV and tumor dosimetry. In addition to dose metrics, the percentage of the tumor volume intersecting with each PV was computed. Using the example case above, both tumors had 100% intersection with all PVs analyzed in the axial slice shown.

	Closest Match to CBCT Method		
	No. of Cases		
	10 pct	20 pct	30 pct
PV (mL)	14 (33%)	17 (40%)	11 (26%)
PV Dose (Gy)	18 (43%)	14 (33%)	10 (24%)
Tumor Dose (Gy)	11 (26%)	17 (40%)	15 (36%)
Tumor D_{95} (Gy)	11 (26%)	18 (43%)	14 (33%)

Table 1 (left) Number and % of cases where each SPECT threshold aligned most closely with the CBCT PV volume. Which SPECT threshold is best? No clear answer – case dependent. CBCT is also not necessarily the ground truth, but which SPECT threshold aligns best seems generally random. The 20% SPECT threshold did show the most common alignment with CBCT.

Figure 2 (below) Bland-Altman style plots showing differences in PV mean dose between CBCT and SPECT segmentation methods. The data are plotted relative to CBCT PV size. The variability in PV dose differences increased from 10 pct to 20 pct to 30 pct thresholds. This was mainly due to the trend toward much smaller volumes at higher thresholds for segmentation. Some cases showed dramatic differences on the order of thousands of Gy.



Standard Recon	^{90}Y-SPECT vs. CBCT Contours					
	Median Difference			Range		
	10 pct	20 pct	30 pct	10 pct	20 pct	30 pct
PV (mL)	35.2	-7.6	-23.1	-84.8 – 311	-175 – 154	-195 – 57.6
PV Dose (Gy)	-250	136	772	-1810 – 1760	-1230 – 4470	-714 – 8220
Tumor Dose (Gy)	-396	-23.6	449	-2760 – 1320	-1920 – 2700	-1190 – 5670
Tumor D_{95} (Gy)	-162	-14.8	204	-2030 – 1240	-1410 – 967	-1100 – 3420
Monte-Carlo Recon	10 pct	20 pct	30 pct	10 pct	20 pct	30 pct
PV (mL)	22.1	-12.2	-25.2	-104 – 173	-182 – 65.5	-204 – 29.2
PV Dose (Gy)	-204	213	920	-1500 – 2500	-1110 – 5330	-812 – 9070
Tumor Dose (Gy)	-351	143	899	-2850 – 1800	-2220 – 3040	-1120 – 5210
Tumor D_{95} (Gy)	-252	-21.4	333	-2000 – 409	-1500 – 778	-656 – 3210

Table 2. Differences in PV, PV mean dose, tumor mean dose, and tumor D_{95} between CBCT and SPECT segmentation. On average, the 20 pct threshold was the closest to CBCT. Case-specific variations were not predictable overall. Each threshold aligned best with CBCT in multiple specific cases.

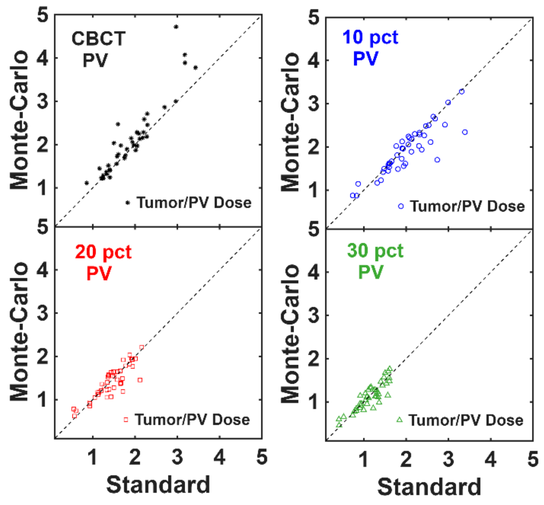


Figure 3. Plots showing the correlation between standard and MC-SPECT recons for tumor mean dose/PV mean dose ratios. With equivalent PV size in CBCT, the MC recon generally produces higher tumor dose relative to PV dose. But with changing PV size using thresholds, more cases display a lower tumor dose relative to PV dose with the MC corrected recon. This is explained by the fact that MC-SPECT generally confines counts to smaller volumes with less blurring.

Model	Dose-Response Predictions			
	Complete Response		Partial Response	
	N	Mean Prob	N	Mean Prob
PV Mean Dose	35/35	0.88	0/5	≥0.77
CBCT Tumor Mean Dose	34/35	0.93	3/5	0.50
10 pct Tumor Mean Dose	33/35	0.91	2/5	0.61
20 pct Tumor Mean Dose	34/35	0.91	1/5	0.65
30 pct Tumor Mean Dose	35/35	0.91	0/5	0.66
CBCT Tumor D_{95}	34/35	0.96	4/5	0.27
10 pct Tumor D_{95}	34/35	0.95	3/5	0.33
20 pct Tumor D_{95}	34/35	0.95	3/5	0.32
30 pct Tumor D_{95}	34/35	0.93	3/5	0.46
30 pct PV Mean Dose + 20 pct tumor intersection	**35/35**	**0.98**	**4/5**	**0.16**

Table 4. Prediction results from dose-response models using various dose metrics. All models using PV mean dose predicted complete response for all tumors despite 5 tumors with partial response. CBCT tumor D_{95} predicted 38/40 tumors correctly. But PV mean dose using 30 pct SPECT thresholds and tumor volume intersecting with 20 pct threshold PV was the best performing model. Such a model would not require full, voxelized dosimetry and could be implemented easily.

CONCLUSIONS

- PV size varied significantly based on segmentation method, with only a single SPECT-threshold version being statistically comparable to CBCT (20 pct standard recon, p=0.152)
- Despite the wide variations in absolute values for dose metrics, dose-response models generally performed comparably across all segmentation methods
- The primary differences were observed in predicting tumors that would not fully respond: only certain models were able to identify these tumors (n=5 out of 40), most often using tumor D_{95} as the primary dose metric
- The percentage of tumor volumes within ^{90}Y-SPECT threshold PVs could be combined with PV dose metrics to help improve predictions for cases with a high risk of incomplete response
- Such an approach could be easily incorporated into post-therapy assessment without requiring significant efforts traditionally tied to 3D, voxelized dosimetry
- The results in this study highlight that post-therapy ^{90}Y-SPECT can help identify discrepancies between planned and delivered volumes, while also informing adequate tumor alignment within treated regions